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Dementia Precox Studies

THE ADRENAL MYDRIASIS OF DEMENTIA PRECOX.

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Any new test leading to diagnosis or directing efforts toward research in this grave and too prevalent disease is most welcome. There has been much written of a predementia precox condition based largely on opinion and conjecture, depending mostly on mental manifestations and errors of conduct. Such articles are confusing to the mechanistic pathologist, but they do emphasize the desirability of early recognizing the origin of the predementia precox "shut in personality." Is it a chemical condition or a mental twist? It is with no expectation of solving the problem that the evidence and accumulated facts of biochemistry are here presented. Facts are relative and valueless unless their relation to some human need is conceived by the imagination and utilized by the untiring will. These facts are presented with a prejudice—a positive prejudice—a human prejudice born of living, knowing, suffering and doing—a prejudice in the consistency of nature and the inexhaustible cunning of the human mind to solve nature's problems for human good. And this is one.

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After reading the recent contribution of J. H. Schultz (Monat. f. Psy. u. Neur., 1915, xxxvii, 205-227) and the little treatise of Richard Cords, of Bonn (Die Adrenalinmydriasis und ihre diagnostische Bedeutung, 1911), we find ourselves possessed of a new diagnostic symptom in cases of dementia precox or cases where the diagnosis lies between this condition, with its melancholy prognosis, and more hopeful diseases. In the great bulk of healthy persons and sick people as they come to the clinic, there is no reaction of the pupil to 1:1000 adrenalin solution instilled into the conjunctival sac. Even if this is repeated for three or four times, at intervals of two or three minutes, there is no mydriasis at the end of ten minutes, a half hour, an hour, or any longer time.

In cases of indubitable dementia precox, however, mydriasis comes on at the end of ten minutes and it persists for half an hour or even longer. Out of sixty cases of dementia precox examined by Schultz, fourteen gave a negative reaction, twenty-eight were very strong positive, seven showed mild mydriasis, while eleven exhibited the paradox of a pupillary contraction.

In order to understand at all the significance of this test upon the pathology of dementia precox it is necessary for us to consider briefly, though incompletely, the history of ocular adrenalin reactions.

In 1898, Max Radziejewski (Berl. klin. Wchnschr., 1898, xxxv, 572) reported the instillation of a ten per cent extract of the adrenal into the conjunctival sac of 500 patients. He noticed no dilatation of the pupil and no changes in accommodation. About the same time, however, Lewandowsky demonstrated on cats some very valuable facts (Ztschr. f. Physiol., 1898, xii, 599) relative to the action of adrenal extract on the cat's eye. He found that the intravenous injection of adrenal extract produced the same effect as the stimulation of the cervical sympathetic, namely mydriasis, retraction of the nictating membrane, slight protrusion of the globe and slight opening of the lids. With large doses of the extract the mydriasis was maximal, and eserine did not completely obliterate it. This mydriasis appeared in a few seconds after the injection and continued only a few minutes. The mydriasis was synchronous with the "pressor" symptoms, but they showed themselves a little later and passed away more tardily. In rabbits the ocular reactions were less obvious and weaker. When Lewandowsky cut the sympathetic and extirpated the superior sympathetic ganglion, the effect of the injection remained the same. Even a long time after extirpation the reaction remained unchanged. Though electric stimulation of the sympathetic produced the same effect as the intravenous injection of adrenal extract, the effect of the latter was not affected or changed by the extirpation of the superior sympathetic ganglion. Boruttau (Arch. f. d. ges. Physiol., 1899, lxxviii, 97) confirmed these observations and further called attention to the blanching of the conjunctival sac on the instillation of adrenal extract.

Then came the pure adrenalin of Takamine (Therap. Gaz., 1901, xxv, 221-224) to which Aldrich (Am. Jour. Physiol., 1901, v, 457, and vii, 359-68) gave the correct empirical formula, and afterward all the experimental work of Stolz (Ber. d. chem. Gesellsch., 1904, xiv, 4149) and his better known followers, in the synthesis of adrenalin and in the reaction and potency studies of the various modified conditions of this base, both from a chemical and from an optical standpoint, made all research more explicit.

The Meltzers have studied the action of adrenalin on the pupil under almost every conceivable experimental condition. They demonstrated its action on the isolated frog's eye and its use as a test for the efficiency or potency of adrenalin products and solutions. They found the mydriatic action of adrenalin greater after complete extirpation of the superior cervical ganglion than when the subganglion sympathetic was simply cut. These experiments were made on rabbits and after section of the sympathetic a subcutaneous injection of adrenalin in rare instances produced a slight and scarcely recognizable mydriasis which quickly disappeared, but after the extirpation of the ganglion a dose of 0.001 gr. produced a dilatation of the pupil in ten to fifteen seconds that lasted an hour or two. After ganglion extirpation the instillation of adrenalin solution into the conjunctival sac (four or five times, a few minutes apart) produced the maximum mydriasis in two or three minutes, and this was not overcome by eserine and it appeared even if an eserine myosis had been previously established. These effects were first produced twenty-four hours after the excision of the ganglion, and they remained even thirty months later, though somewhat modified and retarded.

During an interval beginning twenty-four hours after extirpation of the pancreas and lasting until sixty-five hours after the operation, Löwi (Wein. klin. Wchnschr., 1907, xx, 782, and also Arch. f. exper. Path. u. Pharmakol., 1908, lix, 83) found that the subconjunctival instillation of 1:1000 adrenalin solution which produced no reaction on normal cats and dogs, and little effect even in guinea pigs and rabbits, produced in the animals from whom the pancreas had been removed a mydriasis beginning in twenty to sixty minutes and lasting six hours. The instillation of eserine still produced prompt myosis, however.

Zak (Verhandl. d. Cong. f. inn. Med., 1908, xxv, 392, and also Arch. f. d. ges. Physiol., 1910, cxxxii, 147) by simply scratching or scarifying the duodenum and its mesentery and the stomach produced adrenal pupillary mydriasis at once after the operation, and he repeated the same condition in man in peritonitis and in one case of meningitis.

This mydriasis seems to be associated with experimental glycaemia for Biedl and Offer (Wien. k. Wchnschr., 1907, xx, 1530) by ligating the thoracic duct and by producing a chylous fistula, produced a glycosuria and a coincident adrenalin pupillary susceptibility and mydriasis.

In trying to measure the significance of the mydriatic phenomena in dementia precox we naturally look, not only to anatomy and physiology, but also to pathology and experimental pathology. In what other conditions are similar phenomena observed?

Bittdorf (Ztschr. f. inner. Med., 1909, xxx, 33) observed an adrenalin mydriasis in a case of facial paralysis, and Cords (his monograph, p. 18) records a case of gunshot wound of the temple, with transitory paralysis of the first branch of the fifth and of the abducens and a complete paralysis of the trochlear and the sympathetic in which he had a mydriasis of the right eye on adrenalin instillation.

Zak (loc. cit. no. 1) reported a carcinoma of the soft palate with metastasis in the lymph glands of the left side of the neck and paralysis of the sympathetic. There was myosis of the left pupil but the instillation of adrenalin solution 1:1000 in both eyes resulted in a maximum mydriasis in the left but no reaction in the right eye.

Gautrelet (Arch. d'opth., 1909, xxix, 222) reported a stab wound of the left side, one centimeter below the lower jaw, with paralysis of one vocal cord, the vagus and the sympathetic. There was retraction of the eyeball and myosis. Four months after the injury both eyes were instilled with three drops of adrenalin solution 1:1000 and there was a slight mydriasis of the left pupil, but two drops more produced, after fifteen minutes, a remarkable mydriasis of the left pupil which continued for half an hour. The identical treatment of the right eye produced no effect.

Cords (loc. cit., p. 53) recounts a parallel experience from the Ophthalmic Clinic of Leipzig. A woman eighty-one years old had been operated years before for a carcinoma of the right cheek and now had a carcinoma of the right orbit. There were several masses on the under border of the bony orbit that rendered the globe practically immovable. There was complete paralysis of the first and second branches of the fifth nerve and ptosis. Vision was sufficient to recognize figures at two yards. The cornea was covered by the upper lid and was normal. There was no vasomotor disturbance. The right pupil was a little slower to light than the left. The left pupil dilated with a three per cent cocaine solution. The right pupil remained unchanged. But after the instillation of both eyes with a 1:1000 adrenalin solution the right pupil, at the end of a half hour, was dilated (6 ccm.) in a bright light while the left was unchanged. It seems likely that the sympathetic was involved by the tumor mass in the orbit itself, perhaps the ciliary ganglion was destroyed.

Cords reports also two other cases of injury at the base of the skull, one from a gun-shot wound and the other from a compound fracture of the base with the destruction of the sympathetic and the appearance of the adrenal pupillary reaction.

Shima and Zak have observed the adrenalin mydriasis in destructive diseases of the brain. Shima (Arch. f. d. ges. Physiol., 1909, cxxvi, 269, and also cxxvii, 99) observed mydriasis after lesions of the frontal lobe and also of the medulla. Zak (Arch. f. d. ges. Physiol., 1910, cxxxii, 147) observed adrenalin mydriasis in two cases of tuberculous meningitis in which the mydriasis was maximal, one case of hydrocephalus, in one case of diffuse sclerosis of the brain, in one case of miliary tuberculosis and in one case of post-encephalitic residue in the brain with epilepsy. Zak discusses the relation of mydriasis to glycosuria.

Zak's experiments on animals and also on men would indicate that a scarifying of the intestine, especially the duodenum, resulted in an adrenalin mydriasis. He injected two dogs with a ten per cent solution of caustic soda into the duodenum and brought about a transitory glycosuria and adrenalin mydriasis. Both symptoms had disappeared by the end of forty-eight hours. Vigorous cauterization of the rectum and large intestine produced no result. In rabbits the maximal adrenalin mydriasis appeared in three-quarters of an hour after the cauterization of the stomach.

In the clinical literature only a few cases of a similar nature have been reported by Zak and Bittdorf. These included pelvic peritonitis from abortion, intestinal obstruction, appendicitis, obstruction of the common duct, carcinoma of the stomach and even ulcer of the stomach. The myosis from morphine did not prevent the appearance of the adrenalin mydriasis.

Besides a few cases of glycosuria and diabetes mellitus a number of instances of disturbances of the glands of internal secretion show this anomaly. Loewi, however, did not find this reaction in a case of diabetes with acromegaly. Epinger, Falta and Rudinger demonstrated this symptom in only four of twenty cases of exophthalmic goitre.

The pupillary reaction in dementia precox is similar to that which occurs when the ciliary ganglion is extirpated (Meltzer) or the superior cervical ganglion is excised.

A similar reaction occurs in cases of hyperglycaemia, in extirpation or destruction of the pancreas, and in irritated conditions of the duodenum and stomach.

The value of this reaction as a means of differential diagnosis may not be great but its usefulness in suggesting the direction of research can hardly be overestimated. When we take into consideration the fact that the blood pressure in dementia precox is always low and that subcutaneous injections of adrenalin do not raise it; when we notice that the Abderhalden reaction indicates a dysfunction of the glands of internal secretion in this disease, especially of the sex glands; when we find that morphologically the sex glands and most of the other glands of internal secretion are obviously dystrophic as shown by modern microscopical methods, when we take into account the secondary origin of most pluriglandular disturbances that we know anything about, such as hypo- and hyperthyroidism and pancreatitis; then we begin to value the disturbances of the glands of internal secretion as promising ultimately a way to discover the infection on which dementia precox depends.

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It is not to the clinical psychiatrist alone that the need of some objective diagnostic symptom complex in dementia precox comes with the strongest urge but to the family physician and the surgeon. In the light of well established pluriglandular dysfunctions which are demonstrated in the great mass of these sick folk after they are committed to public custody, the fruitless efforts of surgeons and quacks to cure are very interesting and often ludicrous. A considerable number of dementia precox patients first go to the physician complaining of abdominal distress with vague or with bizarre indications. Not a few of these turn up in the surgeon's office and from a brief examination and with the prejudiced anamnesis brought by the perfectly honest but confused physician, the surgeon recommends an appendisectomy and too often it is performed. Failing to recognize the significance of the dilated pupil, the low blood pressure, the adrenalin attitude paradox of Ludlum and Corson White or the pressor paradox of Willi Schmidt but appreciating fully the toxic condition of the patient, the grave significance of the history and the every-day probability of appendicitis, even if not overestimating the diagnostic skill of his consultant, the surgeon recommends the operation. In such cases surgeons have not yet come to requiring serologic examinations; especially have they overlooked the great value of the Abderhalden Reaction in such cases.

I cannot better enforce this idea than by reciting some of the incidents connected with a case which lately passed through my hands.

Miss X, twenty-eight years old, had been a healthy girl since birth, with no sickness during all that time that had put her to bed. Her father was a slim, nervous blond of exemplary habits until he was thirty years old and after his family were all born. He was a successful business man but at about thirty or thirty-two he began to drink and lead a fast life, the strain of which he was physically ill-able to endure. He was fond of horses and had a farm where he bred racing stock. While on this farm he suffered a sunstroke when about thirty-five, and died within three days in a delirious condition. The patient's mother, a brunette still living, is of a phlegmatic temperament, stoutly built, calm, self-contained and practical. Our patient resembles her father in form, features and nervous development. She has the artistic temperament, so-called, and has acquired a musical education and has been a professional musician of a high-class for some years. She was thrown out of a position by the European war, but continued to pursue further musical studies in a strenuous manner.

In January of 1915 she had some painful trouble with one of her lower molars. Her dentist was obliged to kill the nerve and early in February made several applications of arsenic to the tooth. The tooth, however, was so painful after these applications that she says she did not sleep for ten nights and ten days. The tooth is now excavated and filled with a temporary cotton antiseptic plug. During March, 1915, she frequently consulted her physician on account of distressing movements in her bowels as she thought. On one of the early examinations there was rigidity, tumor and tenderness in the right iliac region and a leucocytosis of 15,000. There was no swelling about the painful tooth. These symptoms continued during the month in spite of laxatives, the discomfort and distress in the abdomen continued and on at least three occasions the leucocyte count was high. In April the formacations extended to the legs and a vaginal examination discovered a hymen with only a minute perforation. There was no vulvitis, no parasites or other cause discoverable to account for the formacations. At this time the patient confessed anxiety about her sexual disturbances. She had been told by experienced women that she was unnatural in her feelings, and she had worried over this fact very much during the ten days wakefulness with her toothache and subsequently, but not before. Her physician was aroused to the possibility of an oncoming dementia precox, and made every effort to allay her anxiety. The abdominal symptoms took a worse turn and a surgeon was taken in consultation, an appendisectomy was recommended and performed the last week in April. The patient endured the operation bravely and without any disturbance from the anaesthetic. There was scant pathology discovered and the patient's symptoms did not disappear but grew worse. "The elevator of the hospital seemed to pass up and down a second set of legs she felt after the anaesthetic."

On May 31, 1915, I saw her at her home. She was tastily and carefully dressed, and met me with cordial manners and helpful answers to all my questions relative to her personal and family history. She was a moderate blond, tall (five feet, three inches), thin (weight 135 pounds in October, 1914, now 115 pounds), her pupils were widely dilated in front of three open windows and even in the same light in which all other persons in the room had narrow pupils. They responded to sudden, strong light equally but neither pupil contracted when the examining finger touched the sclera. (Westphal-Bumke.) The following chart shows the findings of the following examination.

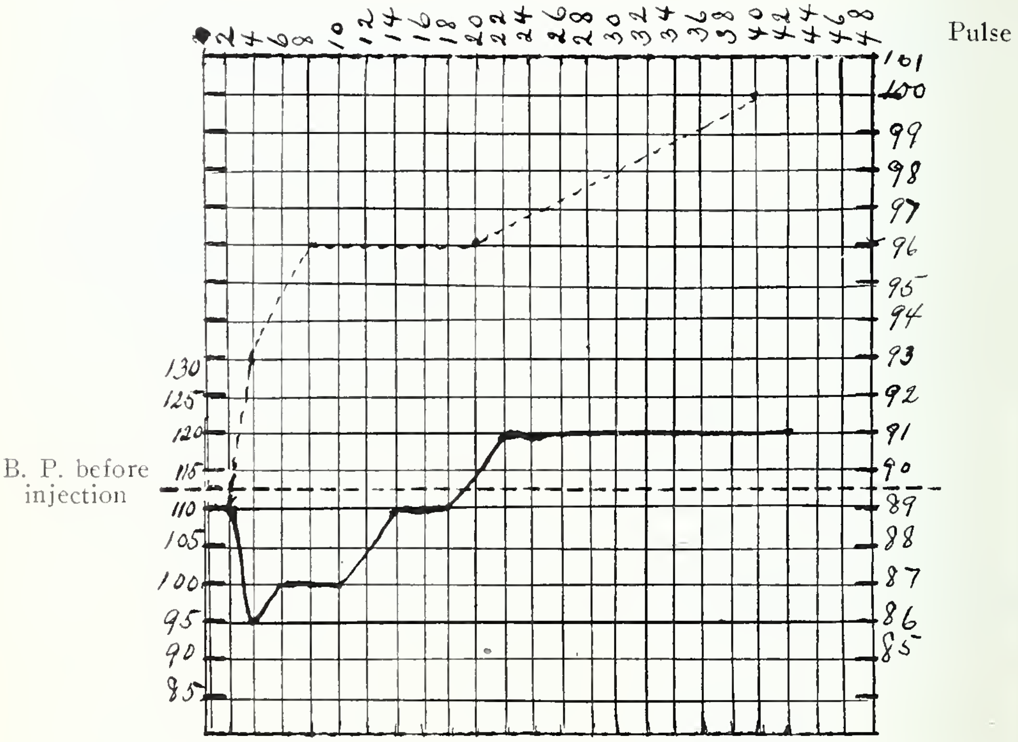
Suggestive Outline of Preliminary Examination of the Adolescent Insane.

Date: June 2, 1915.
Patient: Miss X.
Age: 28.
Circle of chest: 33 inches.
Circle of calf: Scant 12 inches.
Teeth: Regular, fine.
Abdomen: Slight.
Genitals: Imperfect hymen.
Blood examination: Reds, 4,400,000; whites, 10,000.
Examination of the urine: Sp. gr. 1,012; neutral; no albumin, sugar or indican.
Defensive ferment reaction: V. p. 8.

Hour of examination: Between 10 and 12 a. m.
Weight: 115.
Height: 63 inches.
Span: 61 inches.
Form of thigh: Scant: 19½ inches.
Form of lower jaw: Deficient.
Mastoid process: Normal.
Hairiness: Scant.
Breast organs: Normal.
Length of forearm: 9½ inches.
Neck: 12 inches.

Sex Gland	Adrenal	Thyroid	Thymus	Cortex C	Colon	Ilium	Pancreas	Pituitary
+	0	0	—	—	0	—	0	0

Blood pressure before and after injection of adrenalin: 0.5 c.c. adrenalin 1:1000 P. D. Co.'s. Before 0.5 c.c. adrenalin: B. P., sitting, 110; reclining, 115.



Pharmacologic reactions: Tolerance of sugar; sodium nucleate, 10 c.c.=22,000; adrenalin v. chart; eserine.

Susceptibility to other diseases: Never had any. No tonsilitis.

Wassermann reaction: Negative. Oxheart and syphilitic liver, and two other antigens. Two samples taken, one week apart.

Intestinal amines: Betaiminazolylethylamine, 1:500 scratched on arm produced herpes in ten minutes, lasted a half hour.

Abderhalden examination: The blood for this examination was taken from the median vein with a dry needle at ten o'clock on the morning of June 1st, while the patient was still in bed, with a blood pressure of 110 and a normal temperature. She co-operated perfectly in the examination. The blood was centrifuged for a long time, 6 hours, and the serum was put on the substrates (which had been boiled in distilled water and the water found negative to ninhydrin test immediately before using) the same evening. The serum had never been on ice. Three dialysers were used for each substrate, fifteen dialysers in all. After sixteen hours in the incubator at 98.6°, the dialysates were each tested under identical conditions with ninhydrin, and all were — except three that were + + and proved to be from the dialysers containing the ovary:

Control serum alone	—	—	—
Ovary plus 1 c.c. serum	+ +	+ +	+ +
Cerebral cortex plus 1 c.c. serum	—	—	—
Tyhmus plus 1 c.c. serum	—	—	—
Ilium plus 1 c.c. serum	—	—	—

Schultz pupillary reaction: Three drops of an adrenalin solution (1:1000, P. D. & Co.) were instilled into the patient's right eye, while she was lying with the head thrown back. We placed none in the left eye. The lids were raised so as to allow the drops to come in contact with the conjunctiva. This was repeated and the eyes kept closed for ten minutes, when the pupils were again examined. They were unequally but widely dilated. The right eye, however, did not contract as much as the left to strong light but remained for half an hour after quite maximal. This examination was made after the patient had been facing the light of three large uncurtained windows for a half hour and the equal size of the pupils often noticed.

Let us now consider the physical evidences or the objective symptoms this young woman presents of an oncoming dementia precox:

1. The pupils are widely dilated, they respond to light but not to touch on the sclera. (Westphal-Bumke reaction.)

2. The instillation of adrenalin into one eye produced marked mydriasis of the medicated pupil. (Schultz's reaction.)

3. The blood pressure was lower sitting than reclining. (Ludlum-Corson-White's reaction.)

4. The blood pressure was low and 0.5 ccm. of 1:1000 adrenalin solution subcutaneously injected caused it to fall still lower. (Willi Schmidt's reaction.)

5. The defensive ferment capable of catabolizing ovary was present in the blood. (Fauser's reaction.)

Let us note the findings against the diagnosis.

The leucocytes were high. 12-16,000. (This might have been due, however, to the infection of the tooth or to the effect of the recent operation.)

It is then reasonable to diagnose dementia precox.

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Only recently has the full and complete paper of Schultz* come to hand and he has clearly stated the conditions of the test and the results it has yielded in his hands.

In order to make the pupillary adrenalin test as reliable as possible, the patient should be brought before a bright light for ten minutes until the pupillary muscles are quite at equilibrium. Then in the course of five minutes three doses of two drops each of a 1:1000 solution of adrenalin (Schultz used Höchst's sol. suprarenium hydrochlorium, but I should recommend Parke, Davis & Co.'s solution adrenalin 1:1000) is instilled into one eye, and the lids raised so as to bring the solution into contact with the conjunctiva. This often requires much patience with catatonic and restive cases. In these instillations the head is thrown back and when the last one is applied the patient is kept in a reclining position with the eyes closed or covered for ten minutes.

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* Schultz, J. H.: Beiträge zur somatischen Symtomatik und liagnostik der Dementia praecox. Monat. f. Psych. u. Neur., April 1915, xxxvii, 205-226.

The action of the adrenalin on the conjunctiva causes it to become pale and anaemic. When the patient violently closes the eyes during the experiment it may be doubtful if the condition of the pupil has been influenced by the drops. If the conjunctiva has become pale and anaemic the physician may know that in spite of the unfavorable muscular condition of the lids, the adrenalin has had an opportunity to act.

Finally it is important to observe the patients for an hour or more after the experiment. While in sympathetic-paralysis and corneal defects the mydriasis appears quickly; in disturbances of internal-secretion it is visible only after thirty to sixty minutes, as many investigators have noted. In some cases the difference generated in the two pupils remains for days.

Schultz and Cords never noticed any harm to the patients. Post, however, reports frequent cases of severe headache after the instillation; but his is the only report of the kind on record.

In persons who are normal an adrenalin-mydriasis never appears.

Schultz's patients numbered about 150, most of whom had been examined several times. The tabulated results can be more easily read if the cases of organic diseases of the central nervous system are placed first, followed by the various conditions ordinarily considered functional affections.

The results are in agreement with those of Zak (Zak, Emil: Experimentelle und klinische Beobachtungen über Störungen sympathischer Innervationen [Adrenalin-Mydriasis] and über intestinale Glykosurie., Arch. f. ges. Physiol., 1910, cxxxii, 147) Cords (Die Adrenalin-Mydriasis und ihre diagnostische Bedeutung. Bergman, 1911, Wiesbaden), and with other reported clinical findings, as well as with the experiments on animals by Shima; (Uber die Erweiterung der Pupille bei Adrenalin einträufelungen in ihrer Abhängigkeit vom Zentralnervensystem., Arch. f. ges.

INDISPUTABLE ORGANIC DISEASES.

	No. of Cases	M	F	+	?	—	Remarks
Paralysis	9	9	—	4	2	3	
Taboparalysis	2	2	—	—	—	2	
Syphilis of the Brain	3	2	1	—	1	2	
Alcoholism	3	3	—	1	—	2	
Alcoholism plus Korsakoff	1	1	—	—	—	1	
Alcoholism plus Senility	1	—	1	—	—	1	
Cerebral infantile paralysis plus epileptic-trepanation	1	1	—	1	—	—	No positive contralateral influence
Deaf and Dumb from Skull Defect	1	1	—	—	—	1	
Multiple Sclerosis with dementia	2	1	1	2	—	—	
Multiple Sclerosis without dementia	1	1	—	—	—	1	
Advanced Huntington's Chorea	2	2	—	1	1	—	
Senile Dementia	2	—	2	2	—	—	
Totals	28	23	5	11	4	13	

Physiol., 1909, cxxvii, 99) of especial interest is the observation that the senile involution of the brain seems disposed to adrenalin-mydriasis *and still further the positive results in two cases of Huntington's chorea.* There is a suggestion in the conflicting results in pure paralysis, cerebral syphilis and in taboparalysis. At present a discussion of these findings seems premature. They must first be verified in a greater number of experiments. At any rate, of twenty-eight cases of organic brain affection eleven show a certain and four a doubtful adrenalin mydriasis.

Quite different are the results in functional affections. With the exception of dementia precox, which Schultz conservatively, if not naively, classes with the functional affections all were negative except two:

FUNCTIONAL PSYCHOSES AND NEUROSES.

(Excepting dementia precox.)

	No. of Cases	M	F	Results
Epilepsy	9	5	4	all —
Hysteria	9	2	2	all —
Psychopath. Constitution	3	2	1	all —
Imbecility	3	1	2	all —
Imbecility and Hysteria	2	—	2	all —
Melancholia	13	2	11	all —
Manic Psychoses	2	—	2	all —
Cyclothymia Plus Basedowii Plus Degenerative Features	1	—	1	+
Hypochondria Plus Arteriosclerosis	2	2	—	all —
Paranoia	1	1	—	all —
Degenerative Psychoses	3	2	1	(1 + (2 —
Totals	84	18	26	2+46—

The results of these findings are of more value as, with the exception of a few manic cases, Schultz dealt with sane patients, who coöperated willingly and helpfully in the examinations. These pure functional diseases react the same as normal individuals to adrenalin mydriasis. Even in cases of melancholy and hypochondria there were cases complicated with arteriosclerosis but they gave no reaction. The two positive cases need a brief discussion.

(1) The positive adrenalin mydriasis in a cyclothymia with Basedow's disease is, according to results from allied cases—manic, melancholic, hypochondriac—very probably due to internal secretory disturbances; the patient was a woman thirty years old. She had a struma with slight exophthalmus, a tremor, occasional tachychardia and definite vasomotor disturbances. The blood picture revealed a distinct mononuclear leucocytosis. The psychic picture was governed by changing depressions, mostly exogenous, complicated with many symptoms of hysteria; a hypomanic constitution which is very evident during the intervals between periods of depression. The case is one lying between the degenerative and manic depressive groups.

(2) It is equally interesting to notice that the second case also presents a picture of degeneration. A forty-year-old woman had returned to the clinic several times since 1898. She came of a degenerative stock and had at her various visits to Schultz's clinic presented changing pictures of acute confusion, sometimes worried, sometimes cheerful in color, periods of elation, severe emotional excitement due to a psuedo-asthmatic syndrome, excessive loss of hair and epileptic-like attacks. During the free periods she was orderly, intelligent and industrious. "From the fluctuations of the above disease picture, as well as from the symptomatic polymorphic and the proteus-like inconstancy and vague clinical pictures it is possible to conclude that she is a degenerative with constitutional psychosis."

Both cases showed thyroid catabolism in the Abderhalden reaction and are similar to cases described in Fauser's early papers. The following table shows the pupillary reaction of the sixty cases of dementia precox examined by Schultz.

DEMENTIA PRECOX PATIENTS.

	No. of Cases	Mydriasis		Paradox	No Reaction
		+	+?	Pupil Contracted	
Positive Cases............	19	8	2	4	5
Positive Cases............	34	20	5	7	2
Doubtful Cases............	4	0	0	0	4
Doubtful Cases............	3	0	0	0	3
Totals................	60	28	7	11	14

Of fifty-three indubitable cases of clinical dementia precox, twenty-eight show a definite, some of them an unusually strong, adrenalin mydriasis, seven are doubtful, seven are unmoved. Besides these there are seven clinically doubtful cases of dementia precox, all of which are negative.

SUBDIVISIONS OF DEMENTIA PRECOX.

	No. of Cases	++	+	+?	Paradox	No Reaction
Hebephrenie	22	1	10	4	4	3
Catatonia	20	3	8	1	4	4
Dementia Precox Simplex plus Paranoia	8	0	5	2	0	1
Acute	8	2	4	1	1	0
Chronic	42	2	19	6	7	8
Totals	100	8	46	14	16	16

Previous medication of the patient Schultz asserts is without influence on the pupillary reaction. This is in accord with the statement of research workers, that even in deep narcosis the adrenalin mydriasis may be produced in the proper animal.

It is an interesting fact that a number of dementia precox cases give the "paradox reaction" to adrenalin instillation; that is to say, the pupils contract instead of dilating. They are cases that already have only half-dilated or less than half-dilated pupils. In the same way, according to Falta, Newburgh and Nobel (Wechselwirkung der Drüsen mit innerer Sekretion. Zeit f. klin. Med., 1911, lxxii, 97) diabetic patients react to thyroid feeding with a fall of blood pressure in sharp contrast to the rise in blood pressure appearing in normal individuals. Dale (Jour. of Physiol., 1906, xxxiv, 163) has shown that animals poisoned with ergotoxin preparations no longer react to adrenalin with a rise of blood pressure but often with the reverse, a fall of blood pressure. This is exactly the condition found in most cases of clinical dementia precox, as shown by Willi Schmidt. Accordingly, in the cases reacting paradoxically to adrenalin one could hypothetically estimate the existence of an endogenous poison related physiologically to ergotoxin.

CONCLUSIONS AND INDICATIONS.

1. The study of dementia precox patients should be conducted in every stage of its protracted and varied course on rational and mechanistic principles such as prevail in the study of sicknesses not accompanied by mental disturbances or errors of conduct.

2. The early removal of these patients; mostly youths of high school age from the care of the general practitioner and the ordinary medical

profession to the state custodial asylums and private mad houses does not relieve the organized profession of the moral obligation to solve this problem, using such means and methods as have been effective in the solution of other problems of like or similar nature.

3. The evidences presented here and in previous studies are adequate to demand of the medical profession a concerted effort to solve this dark problem and to offer some suggestions of the direction which research should follow.

4. This work has its natural place in the state hospitals. The paralyzing pessimism, the pseudo-scientific nihilism and the fantastic mysticism which has so long dominated our custodial asylums could not withstand a concerted demand for research into the cause of that insanity that takes 15,000 youths each year into hopeless custody.

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